Relapsing polychondritis and myelodysplasia

M. J. Wright¹, K. Bel’eed¹, L. Sellars¹ and I. Richmond²

¹Renal Unit, Hull Royal Infirmary, Hull; ²Department of Pathology, Castle Hill Hospital, Cottingham, UK

Key words: relapsing polychondritis; myelodysplasia; acute renal failure

Introduction

Relapsing polychondritis (RP) is characterized by progressive inflammatory destruction of glycosaminoglycans-containing tissues throughout the body. It typically presents in late middle-age with recurrent painful swelling of the external ear or nose and is often associated with an asymmetrical, non-erosive seronegative polyarthritis, uveitis, episcleritis, or hearing loss.

We report this case to highlight this rare condition as a cause of renal failure. The diagnosis can be difficult to make when the presentation is atypical or the characteristic changes in the nasal cartilage or external auditory meatus are absent. In addition we suggest that there may be a connection between relapsing polychondritis and myelodysplasia.

Case report

A 65-year-old man had a long history of a seronegative polyarthritis. He had more recently developed gout (confirmed by the presence of uric acid crystals in synovial fluid), which was treated with colchicine. A particularly severe episode precipitated hospital admission. His serum uric acid level was 0.45 mmol/l (0.21–0.42). The presence of an erythematous maculopapular rash over the shins and forearms and moderate thrombocytopenia (platelet count = 78 × 10⁹/l) were noted and attributed to colchicine. This was replaced by a combined preparation of diclofenac and misoprostol and he was discharged.

Four days later he was readmitted with acute dyspnoea. He was unable to speak, but his family reported that he had noticed hoarseness for the preceding week which had become much worse on the morning of admission. On examination he had a marked stridor.

Flexible laryngoscopy confirmed a bilateral vocal cord paresis. The arytenoids and aryepiglottic folds were very oedematous. An emergency tracheostomy and laryngeal biopsy were performed. His condition stabilized and intravenous antibiotics and hydrocortisone were given.

The platelet count fell to 59 × 10⁹/l, he was oliguric and fluid overloaded. The serum creatinine rose to 306 μmol/l, having previously been normal. Urine microscopy confirmed the presence of red cells, but there were no casts or urate crystals. Abdominal ultrasound was normal. It was felt that the most likely cause of the worsening renal function was diclofenac exposure so this was withdrawn. A diuresis was successfully induced by administration of frusemide.

There was marked improvement over the following week; the creatinine returned to normal, the platelet count rose to 134 × 10⁹/l, the arthritis and rash improved and there was sufficient resolution of the laryngeal oedema to allow successful closure of the tracheostomy.

Unfortunately, 7 days later, a pyrexia and recurrence of the joint swelling heralded a deterioration. There was a fall in urine output, the rash reappeared and he became confused. The platelet count dropped again and, on this occasion, was accompanied by a fall in the haemoglobin. The blood film, which had previously shown only thrombocytopenia, now showed marked dysplasia of the neutrophils and giant dysplastic platelets. These findings were in keeping with myelodysplasia.

A bone marrow biopsy was performed. This revealed a normocellular marrow with gross dysplasia of all three cell lines. Blast cells accounted for less than 5% of the slide. There were normal sideroblast numbers with occasional ring forms. In addition there were an excessive number of plasma cells (15% ANC) including some blasts.

There was little improvement despite maximal supportive care and, after discussion with the relatives, active treatment was withdrawn. The patient developed bronchopneumonia and died soon after.

The battery of tests performed during life had failed to provide a unifying diagnosis. The laryngeal biopsy showed a non-specific inflammatory cell infiltrate. Autoantibodies were negative but there was an acute
phase response with an ESR of 106 mm/h and C-reactive protein of 56 mg/l. Complement levels were at the upper limit of normal. IgG immune complexes were mildly elevated at 167 \mu g/l (13 to 147 \mu g/l), whilst IgM complexes were present at a reduced level of 4 \mu g/l (9–77 \mu g/l).

Gross examination at autopsy confirmed the presence of bronchopneumonic consolidation of the right upper lobe. The larynx appeared grossly normal and showed no mucosal abnormality. Bilateral pleural effusions and fine pericardial adhesions were noted in keeping with renal failure. Both kidneys were of normal size but showed diffuse cortical pallor. The spleen (530 g) was enlarged and had a soft fluid cut surface in keeping with sepsis. The vertebral marrow had a soft red cut surface.

Histological examination confirmed the presence of myelodysplastic changes within the vertebral marrow (Figure 1). Sections of kidney showed no features to indicate amyloidosis, multiple myeloma or gout.

Within the larynx there was evidence of extensive active chronic inflammation located predominantly in the deeper tissues and particularly at the perichondral aspect of the laryngeal cartilage. This was associated with fibrinoid necrosis and degeneration of some of the chondrocytes (Figure 2). MSB staining for fibrin was strongly positive. The appearances were those of relapsing polychondritis. There was no evidence of vasculitis, mucosal involvement, or neoplasm, though the surrounding laryngeal muscle appeared scarred and fibrotic, suggesting that the process was long standing.

**Discussion**

Our patient presented a considerable diagnostic challenge. Many of his signs and symptoms, such as his rash, thrombocytopenia and transient renal impairment, could be attributed to drug reactions. His arthropathy could be explained as gout superimposed on chronic osteoarthritis. There was no history of swelling of the nose or external ear. Only the laryngeal cord palsy could not be satisfactorily explained until the post-mortem.

The diagnosis of relapsing polychondritis is based upon criteria devised by McAdam et al. [1] and modified by Damiani and Levine [2]. The laryngeal involvement with typical histological changes confirm the diagnosis. The long-standing seronegative arthropathy may have been a manifestation of polychondritis or simply osteoarthritis. The skin rash and renal impairment are both compatible with the diagnosis, but are not part of the diagnostic criteria.

Respiratory tract damage is the presenting feature
in 15% of cases. Tracheostomy is required in up to 80% of these patients. When airway involvement is the dominant feature, the prognosis is poor [3].

Renal involvement is believed to be the result of circulating immune complexes which can produce various histological appearances, ranging from mesangial proliferation to a segmental, necrotizing glomerulonephritis with crescent formation. Renal involvement is another indicator of poor prognosis and is often associated with systemic vasculitis and arthritis [4].

Treatment strategies for this condition are based on isolated case reports and studies of small groups of patients. Non-steroidal anti-inflammatory agents are useful in the treatment of joint symptoms. Dapsone was found to be more effective for systemic disease, although the high incidence of haemolytic anaemia limits its usefulness. High-dose prednisolone has been shown to be particularly effective in reducing upper airway obstruction due to laryngeal inflammation [5]. Steroids are widely used to suppress acute exacerbations but are of uncertain benefit as a long-term treatment. Azathioprine, cyclosporin A, and cyclophosphamide have all been used with some success to treat vasculitic phenomena or as steroid-sparing agents.

An association between relapsing polychondritis and haematological malignancy is not documented in most publications yet a review by Michet et al. [3] found myeloproliferative or myelodysplastic conditions to be the third most common coexisting illness after systemic vasculitis and rheumatoid arthritis. Six patients of 112 had ‘dysmyelopoietic or myeloproliferative’ disorders. One of these died from aplastic anaemia, one from acute myeloid leukaemia, and another (with chronic myeloid leukaemia) from sepsis whilst receiving steroids for RP.

Myelodysplasia may have been responsible for the development of gout 12 months earlier. The changes in the peripheral blood film that occurred during his hospital stay imply that the dysplastic process was moving to a more aggressive phase. The acute flare of RP that occurred simultaneously causing vocal cord paresis, rash, arthropathy, and (we assume) renal impairment suggests that there may be a link between the two conditions.

The mechanism for this is unclear and, given the rarity of RP, difficult to prove. There is evidence that RP is modulated by a humoral factor. IgG antibodies to type II collagen have been detected in the blood of some, but not all, patients. These antibodies are also present in some other autoimmune conditions [6], which may or may not coexist with RP. It is possible that the term relapsing polychondritis encompasses
Relapsing polychondritis and myelodysplasia

several discrete conditions which are regulated by different factors. To confirm this a further review of case histories is required to look for similarities between modes of presentation, related diseases, and response to treatment.

References


Received for publication: 17.3.97
Accepted: 26.3.97